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10/527,455	10/24/2005	Kozo Takeda	TAKEDA19	2196

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EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,455	TAKEDA ET AL.	
	Examiner	Art Unit	
	SHERIDAN SWOPE	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5 and 8-22* is/are pending in the application.

4a) Of the above claim(s) *8,11-16,21 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,5,9,10 and 17-20* is/are rejected.

7)☒ Claim(s) *9 and 18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *0806;0507;0707;0808*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1652, Examiner Sheridan Swope.

The elected invention is directed to a method for removing DNA contaminants from a sample comprising an active protein, wherein the method comprises forming DNA particles in a low conductivity and low pH solution (Applicants' response of August 29, 2007). Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicants' Request for Continuing Examination of December 24, 2008 is acknowledged. It is acknowledged that Claims 1, 4, and 19 have been amended. Claims 1, 4, 5, 8-22 are pending. Claims 8, 11-16, 21, and 22 were previously withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 1, 4, 5, 9, 10, and 17-20 are hereby reexamined.

Priority

The priority date granted for the instant invention is September 11, 2003, the filing date of PCT/JP03/11642, which disclosed the elected invention. If Applicants wish to perfect their claim of priority to JP 2002-265609, filed September 11, 2002, an English-language translation thereof should be submitted.

Information Disclosure Statement

Some references listed in the Information Disclosure Statement filed May 23, 2007 have not been completely considered. Reference AG has not been considered at all, as it is in

Japanese; while, for references AF, AI, AJ, and AK, only the English-language abstract have been considered (see marked up IDS). The Information Disclosure Statement has been placed in the application file, but the information referred to in said references has not been considered in whole. If Applicants wish for said references to be considered in whole, a supplemental Information Disclosure Statement should be submitted with the English-language translations of references AF, AG, AI, AJ, and AK. Any subsequent rejection, based on consideration of the supplemental Information Disclosure Statement, will not be considered new grounds for rejection.

Title

The title is objected to because it is not sufficiently descriptive of the elected invention.

Abstract

The abstract is objected to. MPEP 608.01(b) states:

> The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

Claims-Objections

Claim 9 is objected to for "treatment of removal", which should be "treatment for removal".

Claims 18 and 20 are objected to for reciting non-elected subject matter.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Double Patenting

> The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ormum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).
>
> A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).
>
> An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Claims 1, 4, 5, 9, 10, and 17-20 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1, 3, 5, 6, 8, and 13 of US Patent 7,332,289. Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 1, 4, 5, 9, 10, and 17-20 herein and Claims 1, 3, 5, 6, 8, and 13 of 7,332,289 are both directed to methods for removing DNA contaminants from a sample comprising an active protein, wherein the method comprises forming DNA particles in a low conductivity and low pH solution. The claims differ in that Claims 1, 3, 5, 6, 8, and 13 of 7,332,289 recite methods wherein the precipitation is performed at pH 4-8, while Claims 1, 4, 5, 9, 10, and 17-20 do not specifically recite said range limitation. The claims also differ in that Claims 1, 3, 5, 6, 8, and 13 of 7,332,289 recite methods wherein the protein antibody is first

isolated using affinity chromatography, while Claims 1, 4, 5, 9, 10, 17, 18, and 20 do not specifically recite said step. The portion of the specification in 7,332,289 that supports the recited methods includes embodiments that would anticipate Claims 1, 4, 5, 9, 10, and 17-20 herein, e.g., removing DNA contaminants from a sample comprising an active protein, wherein the method comprises forming DNA particles in a low conductivity and low pH solution, which are also the methods specifically recited in Claims 1, 3, 5, 6, 8, and 13 of 7,332,289. Claims 1, 4, 5, 9, 10, and 17-20 herein cannot be considered patentably distinct over Claims 1, 3, 5, 6, 8, and 13 of 7,332,289 when there are specifically recited embodiments (removing DNA contaminants from a sample comprising an active protein, wherein the method comprises forming DNA particles in a low conductivity and low pH solution) that would anticipate Claims 1, 4, 5, 9, 10, and 17-20 herein. Alternatively, Claims 1, 4, 5, 9, 10, and 17-20 herein cannot be considered patentably distinct over Claims 1, 3, 5, 6, 8, and 13 of US 7,332,289 when there are specifically disclosed embodiments in 7,332,289 that supports Claims 1, 3, 5, 6, 8, and 13 of that patent and falls within the scope of Claims 1, 4, 5, 9, 10, and 17-20 herein, because it would have been obvious to a skilled artisan to modify the methods of Claims 1, 3, 5, 6, 8, and 13 of 7,332,289 by selecting a specifically disclosed embodiment that supports those claims, i.e., removing DNA contaminants from a sample comprising an active protein, wherein the method comprises forming DNA particles in a low conductivity and low pH solution, as disclosed in 7,332,289. One having ordinary skill in the art would have been motivated to do this, because such an embodiment is disclosed as being a preferred embodiment within Claims 1, 3, 5, 6, 8, and 13 of the patent.

Claims 1, 4, 5, 9, 10, 17-20 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1, 4, 5, 7, 8, and 14 of US Application 12/018,688. Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 1, 4, 5, 9, 10, 17, 18, and 20 herein and Claims 1, 4, 5, 7, 8, and 14 of 12/018,688 are both directed to methods for removing DNA contaminants from a sample comprising an active protein, wherein the method comprises forming DNA particles in a low conductivity and low pH solution. The claims differ in that Claims 1, 4, 5, 7, 8, and 14 of 12/018,688 recite methods wherein the precipitation is performed at pH 4-8, while Claims 1, 4, 5, 9, 10, and 17-20 herein do not specifically recite said range limitation. The claims also differ in that Claims 1, 4, 5, 7, 8, and 14 of 12/018,688 recite optionally first converting the sample to an alkaline pH, while Claims 1, 4, 5, 9, 10, 17, and 19 herein do not recite said optional additional step. The portion of the specification in 12/018,688 that supports the recited methods includes embodiments that would anticipate Claims 1, 4, 5, 9, 10, 17, 18, and 20 herein, e.g., methods for removing DNA contaminant from a sample comprising an active protein, wherein the method comprises forming DNA particles in a low conductivity and low pH solution, which are also the methods specifically recited in Claims 1, 4, 5, 7, 8, and 14 of 12/018,688. Claims 1, 4, 5, 9, 10, 17, 18, and 20 herein cannot be considered patentably distinct over Claims 1, 4, 5, 7, 8, and 14 of 12/018,688 when there are specifically recited embodiments (methods for removing DNA contaminant from a sample comprising an active protein, wherein the method comprises forming DNA particles in a low conductivity and low pH solution) that would anticipate Claims 1, 4, 5, 9, 10, 17, 18, and 20 herein. Alternatively, Claims 1, 4, 5, 9, 10, 17, 18, and 20 herein cannot be considered patentably distinct over Claims 1, 4, 5, 7, 8, and 14 of

12/018,688 when there are specifically disclosed embodiments in 12/018,688 that supports Claims 1, 4, 5, 7, 8, and 14 of that application and falls within the scope of Claims 1, 4, 5, 9, 10, 17, 18, and 20 herein, because it would have been obvious to a skilled artisan to modify the methods of Claims 1, 4, 5, 7, 8, and 14 of 12/018,688 by selecting specifically disclosed embodiments that supports those claims, i.e., methods for removing DNA contaminant from a sample comprising an active protein, wherein the method comprises forming DNA particles in a low conductivity and low pH solution, as disclosed in 12/018,688. One having ordinary skill in the art would have been motivated to do this, because such embodiments are disclosed as being a preferred embodiment within Claims 1, 4, 5, 7, 8, and 14 of the other application. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4, 5, 9, 10, and 17-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the following reasons.

For Claims 1, 9, 10, 18, the phrase "physiologically active protein-containing sample" renders the claim indefinite. It is unclear whether the protein is active only in the starting sample or both the starting sample and the sample after DNA precipitation. The skilled artisan would not know the metes and bounds of the recited invention. Claims 4, 5, 9, 10, and 17-20, as dependent from Claim 1 and/or 18, are indefinite for the same reason. For purposes of

examination, it is assumed that "physiologically active protein-containing sample" means that protein is active in both the starting sample and the sample after DNA precipitation.

For Claims 1, 18, and 19, the phrase "having a concentration of 100mM or less" renders the claim indefinite. It is unclear what substance is being referred to: the concentration of protein, salt, or some other component or composition? The skilled artisan would not know the metes and bounds of the recited invention. Claims 4, 5, 9, 10, and 17-20, as dependent from Claim 1, 18, and/or 19, are indefinite for the same reason. For purposes of examination, it is assumed that "having a concentration of 100mM or less" means having a concentration of 100mM or less of salt.

For Claims 1, 18, and 19, the phrase "a pH from 4.0 to equal to or lower than the isoelectric point" renders the claim indefinite. It is unclear whether said phrase means "a pH from 4.0 to [some other defined pH] or equal to or lower than the isoelectric point" or "a pH of 4.0 or a pH equal to or lower than the isoelectric point". The skilled artisan would not know the metes and bounds of the recited invention. Claims 4, 5, 9, 10, and 17-20, as dependent from Claim 1, 18, and/or 19, are indefinite for the same reason. For purposes of examination, it is assumed that ""a pH from 4.0 to equal to or lower than the isoelectric point" means "a pH from 4.0 to [less than 7.0] or equal to or lower than the isoelectric point".

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

Claims 1, 4, 5, 9, 10, and 17-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 1, 4, 5, 9, 10, and 17-20 are directed to a genus of methods for removing DNA contaminants from a sample comprising any active protein, wherein the method comprises forming DNA particles in a low conductivity and low pH solution, and wherein the protein remains active after removal of the DNA contaminants. Said genus encompasses methods for removing DNA contaminants from compositions including cell culture lysates, culture medium, and tissue homogenates. The specification teaches no such methods. In addition, the genus encompasses methods for removing DNA contaminants from a sample comprising any active protein, wherein the protein remains active after said removal. The specification teaches only one species of said methods, wherein a specific anti-PTHrP antibody sample is depleted of DNA contaminants. Given this lack of description of representative species encompassed by the genera of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Oxenburch et al, 1965. Oxenburch et al teaches a method for removing DNA contaminants from a bacterial lysate having active proteins, wherein the method comprises forming DNA particles in a low ionic strength, pH 6 solution followed by removing the precipitated DNA particles by centrifugation (Fig 1; pg 1416, parg 11, to pg 1417, parg 3). Although Oxenburch et al does not disclose the acid used for setting their solution to pH 6, more likely than not, they used an acid selected from hydrochloric acid, citric acid, and acetic acid. Therefore, Claims 1, 4, and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Oxenburch et al, 1965.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Oxenburch et al, 1965 in view of Kipriyanov et al, 1999. The teachings of Oxenburch et al are described above. Oxenburch et al does not teach use of their method for removing DNA contaminants from an antibody-comprising sample. Kipriyanov et al teach that recombinant antibody fragments can be produced in bacteria (Sections 4.5-5.2 & 5.4-; Figs 2-5). It would have been obvious to a person of ordinary skill in the art to use the method of Oxenburch et al for removing DNA contaminants from the bacterial-derived antibody-comprising samples of Kipriyanov et al. Motivation to do so is provide by the desire to remove the DNA contaminants, which is advantageous in the

preparation of antibodies for treatment. The expectation of success is high, as Oxenburch et al teach that DNA contaminants can be removed from bacterial lysates and Kipriyanov et al teach that recombinant antibody fragments can be produced in bacteria. Therefore, Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Oxenburch et al, 1965 in view of Kipriyanov et al, 1999.

Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Oxenburch et al, 1965 in view of Somack et al, 1999. The teachings of Oxenburch et al are described above. Oxenburch et al does not teach use of filtration to remove the DNA precipitate. Somack et al teach what was well-known in the art; that a DNA precipitate can be removed by filtration through a filter (Example 1B). It would have been obvious to a person of ordinary skill in the art to combine the teachings of Oxenburch et al and Somack et al, wherein the centrifugation step of Oxenburch et al is replaced with filtration of the DNA precipitate, because said techniques are functionally equivalent. Motivation to do so is provide by the desire to remove the DNA precipitate and the ease of filtration for large numbers of samples. The expectation of success is high, as all methods are well-known in the art. Therefore, Claims 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Oxenburch et al, 1965 in view of Somack et al, 1999.

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Oxenburch et al, 1965 in view of what was well-known in the art. The teachings of Oxenburch et al are described above. Oxenburch et al teaches setting their protein-containing solution to pH 7.0 prior to DNA precipitation but does not teach setting their protein-containing solution to pH 7.5 prior to DNA precipitation. The skilled artisan would know that, for most situations, pH 7.0 and 7.5 are functionally equivalent. Thus, it would have been obvious to a person of ordinary skill in the art

to set the protein-containing solution of Oxenburch et al to pH 7.5 prior to DNA precipitation. Motivation to do so is provide by the desire to remove the DNA precipitate. The expectation of success is high because, for most situations, pH 7.0 and 7.5 are functional equivalents. Therefore, Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Oxenburch et al, 1965 in view of what was well-known in the art.

Claims 9 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Oxenburch et al, 1965 and Kipriyanov et al, 1999 in view of Harlow et al, 1988, as evidenced by Fahrner et al, 1999. The combination of Oxenburch et al and Kipriyanov et al is described above. Said combination does not teach isolation of bacterial-expressed antibodies using protein A-sepharose. Harlow et al teach what was well-known in the art; that antibodies can be isolated using protein A-sepharose, wherein the antibody is eluted using 100mM glycine at pH 3, without salts, followed by neutralization with TrisHCl. It would have been obvious to a person of ordinary skill in the art to combine the methods of Oxenburch et al, Kipriyanov et al, and Harlow et al. In said combined method, the antibody-containing, low salt solution obtained via the method of Harlow et al would be adjusted, using the method of Oxenburch et al, to a low pH in order to precipitate any contaminating DNA. Motivation to do so derives from the desire to remove the DNA contaminants in protein A-sepharose isolated antibodies (see Fahrner et al; Table I). Removal of said DNA contaminants is advantageous in the preparation of antibodies for treatment. The expectation of success is high, as all methods were known in the art. The Office does not have the facilities to determine the DNA concentration of the solution prepared by the method rendered obvious by the combinantion of Oxenburch et al, Kipriyanov et al, and Harlow et al. However, more likely than not, said solution inherently has a DNA concentration

of less than 22.5 pg/ml since, the method is essentially identical to the method disclosed by the instant specification. Therefore, Claims 9 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Oxenburch et al, 1965 and Kipriyanov et al, 1999 in view of Harlow et al, 1988, as evidenced by Fahrner et al, 1999.

Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Oxenburch et al, 1965, Kipriyanov et al, 1999, Harlow et al, 1988, and Fahrner et al, 1999 in view of Sigma, Inc. The combination of Oxenburch et al, Kipriyanov et al, Harlow et al, and Fahrner et al is described above. Said combination does not teach a method wherein the buffer used to adjust the antibody-containing solution to a low pH is an aqueous solution of Tris. Sigma, Inc teach an aqueous solution of 500mM Tris at pH 3.5-5.0. It would have been obvious to a person of ordinary skill in the art that said aqueous Tris solution could be used to adjust the antibody-containing solution of Harlow et al to a low pH. Motivation to do so is provide by the desire to precipitate contaminating DNA, as explained above. Even though Tris is not an optimal buffer for maintaining a solution at an acidic pH (Sigma Buffer Chart), the expectation of success is high, as the aqueous Tris solution of Sigma, Inc is at high concentration (500mM) and acidic pH (3.5-5.0). Therefore, Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Oxenburch et al, 1965, Kipriyanov et al, 1999, Harlow et al, 1988, and Fahrner et al, 1999 in view of Sigma, Inc.

Claims 1, 4, 5, 9, 10, 18, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lydersen et al, 1994 (IDS) in view of Harlow et al, 1988, as evidenced by Fahrner et al, 1999. Lydersen et al teaches a method for removing DNA contaminants from a sample comprising an active antibody, wherein the method comprises forming DNA particles in

a low pH solution and removing the DNA particles by centrifugation (pg 226, parg 2, to pg 227, parg 2). Precipitation at pH 4.2 reduces the DNA concentration to 20pg/ml (pg 226, parg 2). As evidenced by Irvine Scientific (Santa Ana, CA), the low pH, precipitating solution has an ionic strength of 107mM NaCl and 4.2mM KCl (see enclosure). Lydersen et al do not teach using their method, wherein the salt concentration is less than 100mM or less than 50mM. Harlow et al teach what was well-known in the art; that antibodies can be isolated from culture medium using protein A-sepharose, wherein the antibody is eluted using 100mM glycine at pH 3, without salts, followed by neutralization with TrisHCl. It would have been obvious to a person of ordinary skill in the art to combine the methods of Lydersen et al and Harlow et al. In said combined method, the antibody-containing, low salt solution obtained via the method of Harlow et al would be adjusted to a low pH in order to precipitate any contaminating DNA. Motivation to do so derives from the desire to remove the DNA contaminants in protein A-sepharose isolated antibodies (see Fahrner et al; Table I). Removal of said DNA contaminants is advantageous in the preparation of antibodies for treatment. The expectation of success is high, as all methods were known in the art. Therefore, Claims 1, 4, 5, 9, 10, 18, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lydersen et al, 1994 in view of Harlow et al, 1988, as evidenced by Fahrner et al, 1999.

Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Lydersen et al, 1994, Harlow et al, 1988, and Fahrner et al, 1999 in view of Somack et al, 1999. The combination of Lydersen et al, Harlow et al, and Fahrner et al is described above. Said combination does not teach a method wherein the DNA precipitate is removed by filtration through a filter. Somack et teach what was well-known in the art; that a DNA precipitate can be

removed by filtration through a filter (Example 1B). It would have been obvious to a person of ordinary skill in the art to adapt the method rendered obvious by Lydersen et al, Harlow et al, and Fahrner et al to replace centrifugation with filtration of the DNA precipitate because said techniques are functionally equivalent in the method rendered obvious by said combination. Motivation to do so is provide by the desire to remove the DNA precipitate and the ease of filtration for large numbers of samples. The expectation of success is high, as all methods are well-known in the art. Therefore, Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Lydersen et al, 1994, Harlow et al, 1988, and Fahrner et al, 1999 in view of Somack et al, 1999.

Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Lydersen et al, 1994, Harlow et al, 1988, and Fahrner et al, 1999 in view of Sigma, Inc. The combination of Lydersen et al, Harlow et al, and Fahrner et al is described above. Said combination does not teach a method wherein the buffer used to adjust the antibody-containing solution to a low pH is an aqueous solution of Tris. Sigma, Inc teach an aqueous solution of 500mM Tris at pH 3.5-5.0. It would have been obvious to a person of ordinary skill in the art that said aqueous Tris solution could be used to adjust the antibody-containing solution of Harlow et al to a low pH. Motivation to do so is provide by the desire to precipitate contaminating DNA, as explained above. Even though Tris is not an optimal buffer for maintaining a solution at an acidic pH (Sigma Buffer Chart), the expectation of success is high, as the aqueous Tris solution of Sigma, Inc is at high concentration (500mM) and acidic pH (3.5-5.0). Therefore, Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over the

combination of Lydersen et al, 1994, Harlow et al, 1988, and Fahrner et al, 1999 in view of Sigma, Inc.

Allowable Subject Matter

No claims are allowable.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages. It is also requested that the serial number of the application and date of amendment be referenced on every page of the response.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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